

10/572871  
AP2004/030921 US PAT 2006

## **APPENDIX A**

**PCT/US2004/030921  
Article 19 Amendment**



CHOATE HALL & STEWART LLP

10/572871

AP20 REC'D PTO 21 MAR 2006

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From	Nancy J. Hough Foreign Filing Specialist	Number of Pages	25
Date	September 13, 2005	Client Number	2003946-0168
Phone	(617) 248-5188	Operator	Time Sent

**Comments** Applicant: Eisai Co., Ltd.  
Intl. Appln. No.: PCT/US2004/030921  
Claiming priority to: USSN 10/667,864, filed 22 September 2003  
Intl. Filing Date: 22 September 2004  
Title: HEMIASTERLIN DERIVATIVES AND USES  
THEREOF

Please see the attached Letter for PCT Article 19 Amendment of Claims, Statement under Article 19(1), Substitute Sheets, and Appendix A-Marked up copy of claim replacements.

Please acknowledge receipt of these documents.

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10/572871

APPROVED FOR FILING 2006

**ATTORNEY'S DOCKET NO.: 2003946-0168 (HEAT/PCT2)  
IN THE INTERNATIONAL BUREAU (WIPO)**

Applicant: Eisai Co., Ltd.  
Intl. Appln. No.: PCT/US2004/030921  
Claiming priority to: USSN 10/667,864, filed 22 September 2003  
Intl. Filing Date: 22 September 2004  
Title: HEMIASTERLIN DERIVATIVES AND USES THEREOF

**VIA FACSIMILE (#011-41-22-740-14-35)  
CONFIRMATION BY  
INTERNATIONAL COURIER**

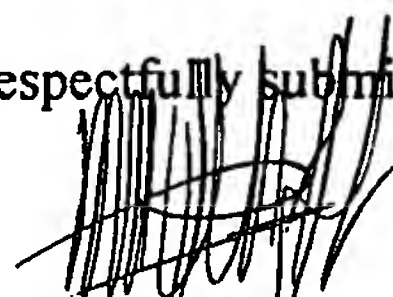
International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20  
SWITZERLAND

**TRANSMITTAL TO THE INTERNATIONAL BUREAU (WIPO)**

Please find enclosed the following documents in the above-referenced application:

1. Letter for PCT Article 19 Amendment of Claims (PCT Section 205) (2 pages);
2. Statement under Article 19(1) (1 page);
3. Substitute Sheets (10 pages, including cover page); and
4. Appendix A – Marked-up copy of claim replacements (10 pages, including cover page).

Respectfully submitted,

  
\_\_\_\_\_  
Nadège M. Lagneau, Ph.D.  
Agent for Applicant  
Reg. No.: 51,908

Date: 13 September 2005

PATENT DEPARTMENT  
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10/5/2871

ATTORNEY'S DOCKET NO.: 2003946-0168 (HEAT/PCT2)

IN THE INTERNATIONAL BUREAU (WIPO) PCT/PTO 21 MAR 2006

Applicant: Eisai Co., Ltd.  
Intl. Appln. No.: PCT/US2004/030921  
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CONFIRMATION BY  
INTERNATIONAL COURIER

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34, chemin des Colombettes  
1211 Geneva 20  
SWITZERLAND

**LETTER FOR PCT ARTICLE 19 AMENDMENT OF CLAIMS  
(PCT SECTION 205)**

1. Applicant herewith submits substitute sheets number 298-300 and 300a-300f to replace sheets number 298-300, originally filed for this application. These substitute sheets are submitted within 2 months of the Notification of Transmittal of International Search Report mailed 13 July 2005.
2. Please delete sheets 284-297, as originally filed for this application, and cancel claims 1-45.
3. In respect of each claim appearing in the international application based on the substitute sheets submitted herewith, and in accordance with PCT Section 205(b), the following claim(s) is/are:
  - (i) Unchanged: Claim 53 is unchanged;
  - (ii) Replaced: Claim 46 is replaced with amended claim 46;
  - (iii) Canceled: Claims 45, 47-52 and 54-61 are canceled;
  - (iv) New: Claims 62-81 are new.

A Marked-up Copy of Claim Replacements highlighting the changes is provided herewith as attached Appendix A. Deletions are represented in square brackets, and additions are represented in underlining. Newly added claims are labeled "New".

101372871

Respectfully submitted,

  
LAP2/HEAT/PCTPTO 21 MAR 2006

Date: 13 September 2005

Nadège M. Lagneau, Ph.D.  
Agent for Applicant  
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CONFIRMATION BY  
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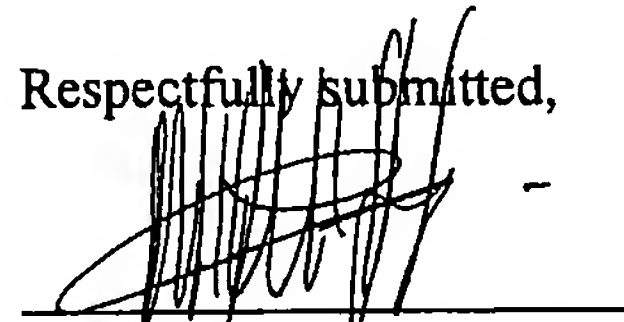
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34, chemin des Colombettes  
1211 Geneva 20  
SWITZERLAND

STATEMENT UNDER ARTICLE 19(1)

Applicant respectfully submits that no new matter is presented with the amendment set forth in the "Letter for PCT Article 19 Amendment of Claims" filed concurrently herewith. Specifically, support for claims 62-65 can be found *inter alia* in Scheme 14 page 105 of the specification as originally filed. Claims 66-68 find support, for example, in paragraph [0124] page 107 of the specification. Claims 69-70 find support, for example, in paragraph [0122] page 106 of the specification. Support for claims 71-77 can be found, for example, in sections d)-j) on page 28 and sections d) and e) on page 29 of the specification. Finally, new claims 62-81 find support *inter alia* in paragraphs [0106]-[0114] on pages 100-104 of the specification as filed.

Applicant respectfully requests entry and consideration of this amendment in processing the application.

Respectfully submitted,



Nadège M. Lagneau, Ph.D.  
Agent for Applicant  
Reg. No.: 51,908

Date: 13 September 2005

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2003/2371

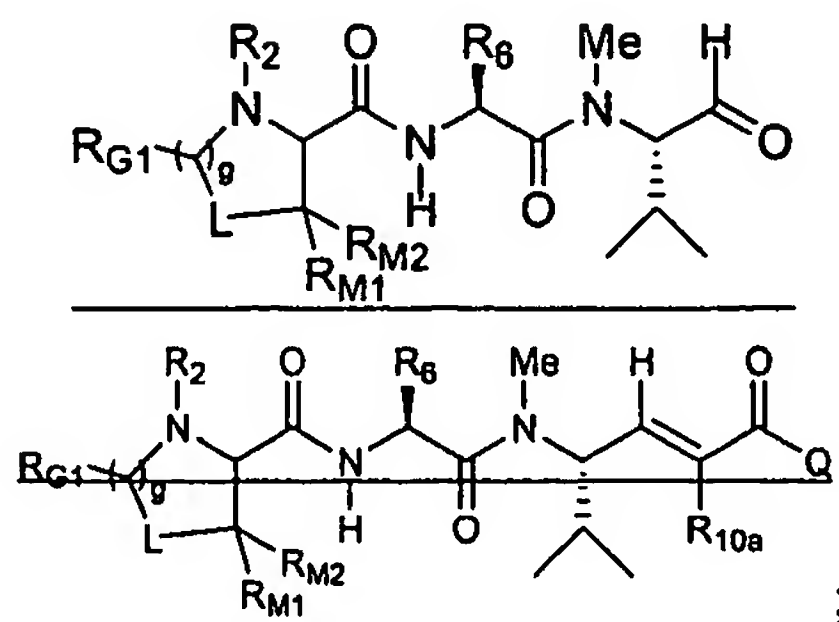
AP20 Rec'd ECTO 21 MAR 2006

- APPENDIX A -

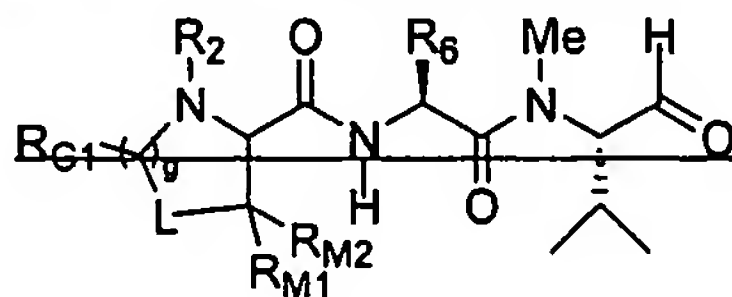
Marked-up Copy of Claim Replacements

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46. **(Currently Amended)** ~~An intermediate for the preparation of a compound~~  
having the structure:



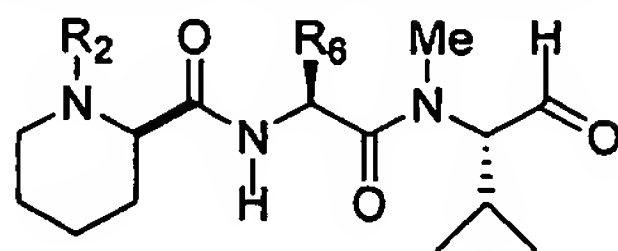
~~wherein said intermediate has the following structure:~~





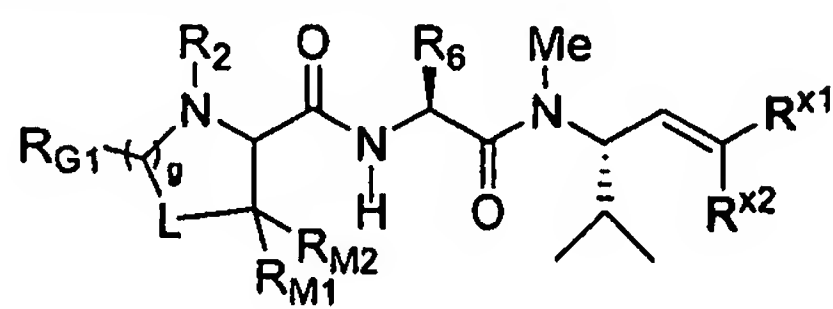
Claims 47-52 (Canceled)

53. (Original) The intermediate of claim 46 having the structure:



Claims 54-61 (Canceled)

62. (New) An intermediate having the structure:



wherein  $R^{x1}$  and  $R^{x2}$  are independently hydrogen, aliphatic, alicyclic or aryl;  
g is 1, 2, 3 or 4;

L is  $CR_{L1}R_{L2}$ , S, O or  $NR_{L3}$ , wherein each occurrence of  $R_{L1}$ ,  $R_{L2}$  and  $R_{L3}$  is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of  $R_{G1}$ ,  $R_{M1}$  and  $R_{M2}$  is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

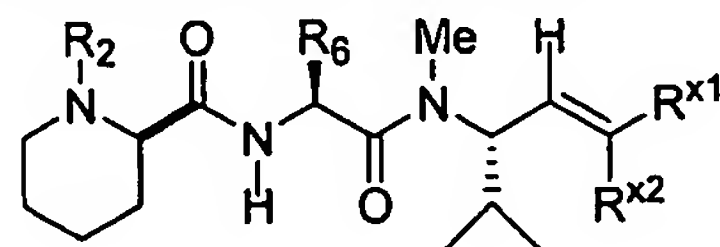
wherein any two adjacent  $R_{L1}$ ,  $R_{L2}$ ,  $R_{L3}$ ,  $R_{G1}$ ,  $R_{M1}$  or  $R_{M2}$  groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety;

$R_2$  is hydrogen,  $-(C=O)R_C$  or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein each occurrence of  $R_C$  is independently hydrogen, OH,  $OR_D$ , or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein  $R_D$  is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

$R_6$  is hydrogen,  $-(C=O)R_E$  or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of  $R_E$  is independently hydrogen, OH,  $OR_F$ , or an aliphatic, alicyclic, heteroaliphatic,

heteroalicyclic, aryl or heteroaryl moiety; wherein R<sub>F</sub> is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety.

63. (New) The intermediate of claim 62 having the structure:



64. (New) The intermediate of claim 62 or 63 wherein R<sup>x1</sup> and R<sup>x2</sup> are independently hydrogen, alkyl or aryl.

65. (New) The intermediate of claim 62 or 63 wherein R<sup>x1</sup> and R<sup>x2</sup> are each hydrogen.

66. (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R<sub>2</sub> is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety.

67. (New) The intermediate of claim 66 wherein R<sub>2</sub> is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -CH(CH<sub>3</sub>)Et, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, -CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, -CH(CH<sub>3</sub>)CH(CH<sub>3</sub>)<sub>2</sub>, -C(CH<sub>3</sub>)<sub>2</sub>Et, -CH(CH<sub>3</sub>)cyclobutyl, -CH(Et)<sub>2</sub>, -C(CH<sub>3</sub>)<sub>2</sub>C≡CH, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.

68. (New) The intermediate of claim 66 wherein R<sub>2</sub> is methyl, ethyl, propyl or *i*-propyl.

69. (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R<sub>6</sub> is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, -CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl; and R<sub>2</sub> is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl, -CH(CH<sub>3</sub>)Et, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, -CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, -CH(CH<sub>3</sub>)CH(CH<sub>3</sub>)<sub>2</sub>, -C(CH<sub>3</sub>)<sub>2</sub>Et, -

CH(CH<sub>3</sub>)cyclobutyl, -CH(Et)<sub>2</sub>, -C(CH<sub>3</sub>)<sub>2</sub>C≡CH, cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.

70. (New) The intermediate of claim 69 wherein R<sub>6</sub> is *tert*-butyl.

71. (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R<sub>G1</sub> is hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.

72. (New) The intermediate of claim 71 wherein R<sub>G1</sub> is hydrogen, methyl or phenyl.

73. (New) The intermediate of claim 71 wherein R<sub>G1</sub> is hydrogen.

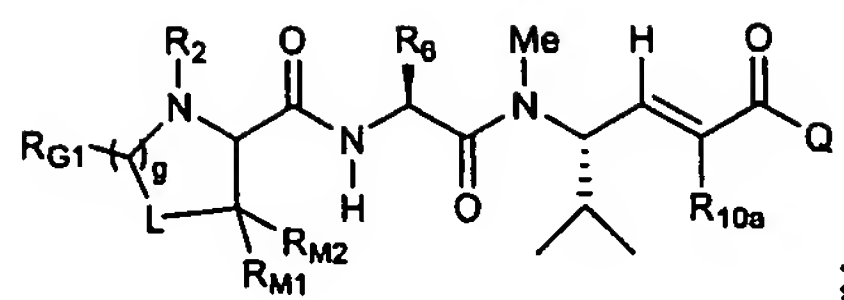
74. (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein R<sub>M1</sub> and R<sub>M2</sub> are each independently hydrogen, hydroxyl, a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl moiety; a substituted or unsubstituted phenyl moiety, or R<sub>M2</sub> is absent when R<sub>M1</sub> and the substituents on L, taken together, form a substituted or unsubstituted aryl or heteroaryl moiety.

75. (New) The intermediate of claim 74 wherein R<sub>M1</sub> and R<sub>M2</sub> are each hydrogen.

76. (New) The intermediate of any one of claims 46, 53, 62 and 63 wherein L is CR<sub>L1</sub>R<sub>L2</sub> wherein R<sub>L1</sub> and R<sub>L2</sub> are each independently hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.

77. (New) The intermediate of claim 76 wherein L is CH<sub>2</sub>.

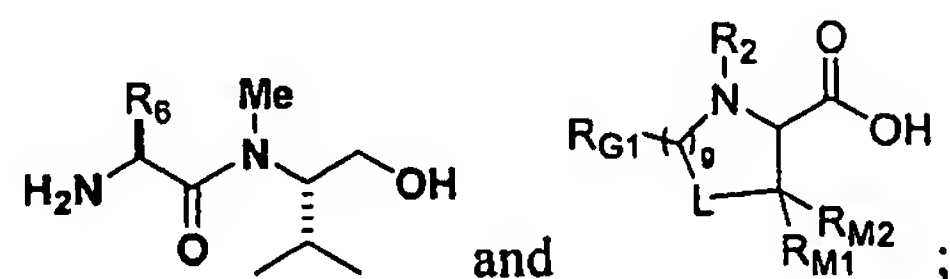
78. (New) A method for preparing a compound of formula VI<sup>A</sup>:



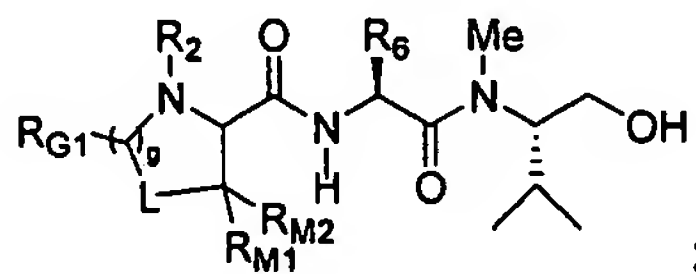
(VI<sup>A</sup>)

said method comprising steps of:

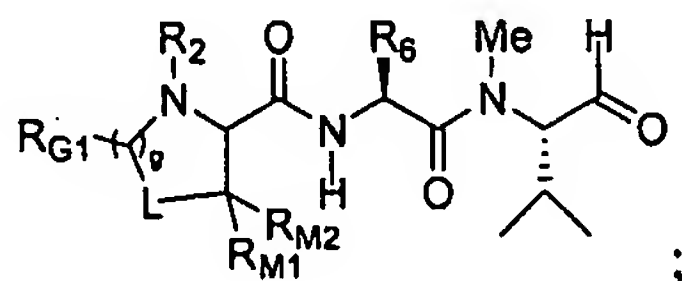
(a) reacting two compounds having the structures:



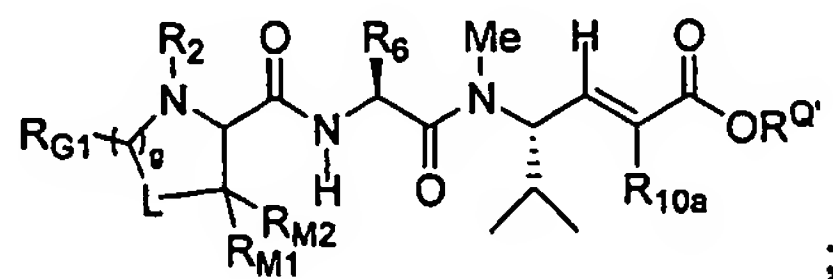
under suitable conditions to form a compound having the structure:



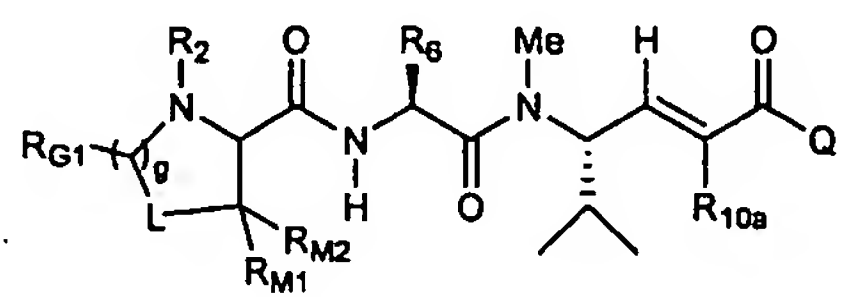
(b) oxidizing the compound formed in step (a) under suitable conditions to form a compound having the structure:



(c) subjecting the compound formed in step (b) to suitable olefin-forming conditions to form a compound having the structure:



(d) subjecting the compound formed in step (c) to suitable diversification reactions to generate the desired compound having the structure:



(VI<sup>A</sup>)

wherein g is 1 or 2;

R<sup>Q</sup> is hydrogen, lower alkyl or an oxygen protecting group;

R<sub>2</sub> and R<sub>6</sub> are independently substituted or unsubstituted linear or branched lower alkyl;

R<sub>10a</sub> is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is CR<sub>L1</sub>R<sub>L2</sub>, S, O or NR<sub>L3</sub>, wherein each occurrence of R<sub>L1</sub>, R<sub>L2</sub> and R<sub>L3</sub> is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

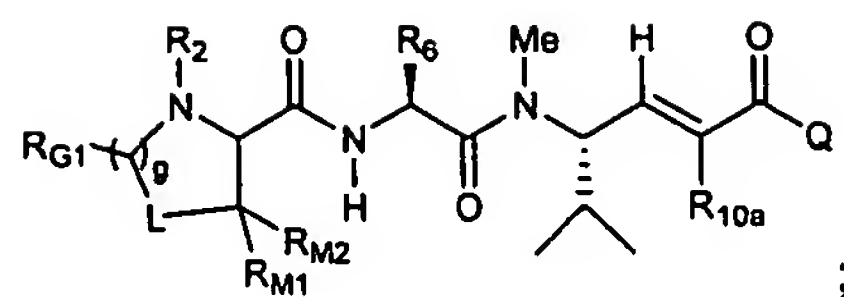
each occurrence of R<sub>G1</sub>, R<sub>M1</sub> and R<sub>M2</sub> is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent R<sub>L1</sub>, R<sub>L2</sub>, R<sub>L3</sub>, R<sub>G1</sub>, R<sub>M1</sub> or R<sub>M2</sub> groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

79. (New) The method of claim 78 wherein, in the step of oxidizing, the conditions comprise Swern or Dess Martin oxidizing conditions.

80. (New) The method of claim 78 wherein, in step (c), the olefin-forming conditions comprise Ph<sub>3</sub>P=C(R<sub>10a</sub>)CO<sub>2</sub>R<sup>Q</sup>; wherein R<sup>Q</sup> is hydrogen, lower alkyl or an oxygen protecting group; and R<sub>10a</sub> is as defined generally above and in classes and subclasses herein.

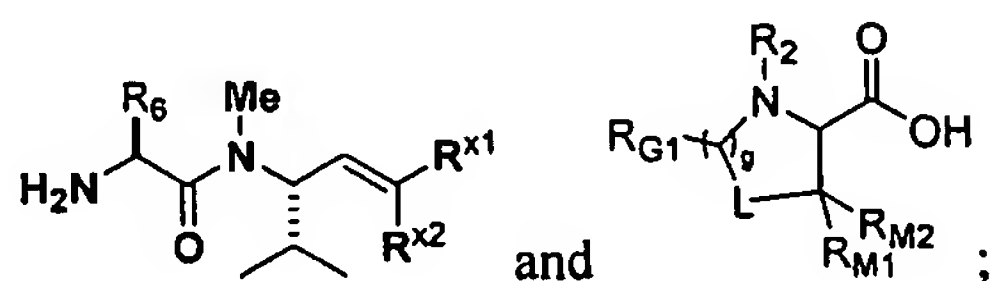
81. (New) A method for preparing a compound of formula VI<sup>A</sup>:



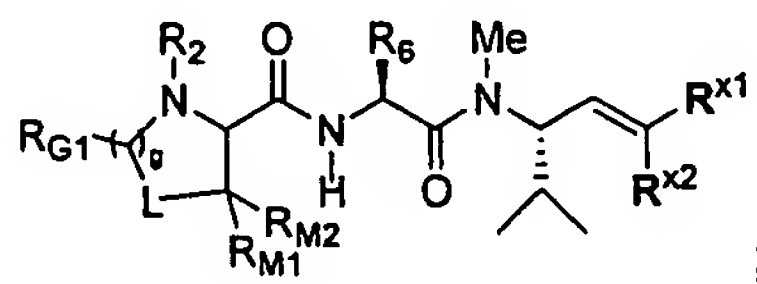
(VI<sup>A</sup>)

said method comprising steps of:

(a) reacting two compounds having the structures:

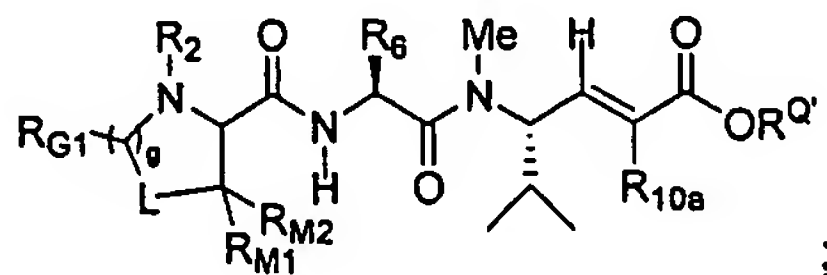


under suitable conditions to form a compound having the structure:

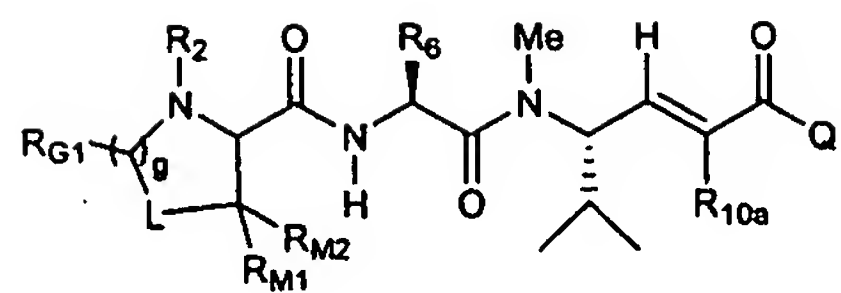


wherein R<sup>x1</sup> and R<sup>x2</sup> are independently hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;

(b) converting the compound formed in step (a) under suitable conditions to form a compound having the structure:



(c) subjecting the compound formed in step (b) to suitable diversification reactions to generate the desired compound having the structure:



(VI<sup>A</sup>)

wherein g is 1 or 2;

R<sup>Q</sup> is hydrogen, lower alkyl or an oxygen protecting group;

R<sub>2</sub> and R<sub>6</sub> are independently substituted or unsubstituted linear or branched lower alkyl;

R<sub>10a</sub> is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

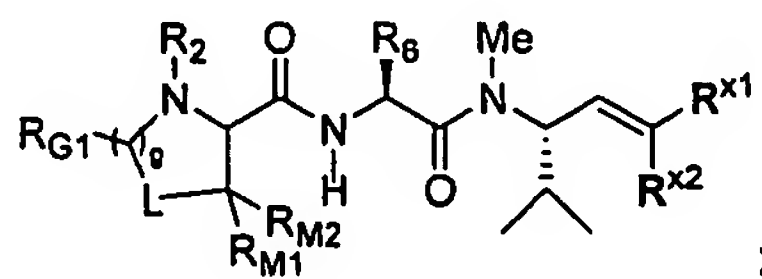
L is CR<sub>L1</sub>R<sub>L2</sub>, S, O or NR<sub>L3</sub>, wherein each occurrence of R<sub>L1</sub>, R<sub>L2</sub> and R<sub>L3</sub> is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R<sub>G1</sub>, R<sub>M1</sub> and R<sub>M2</sub> is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

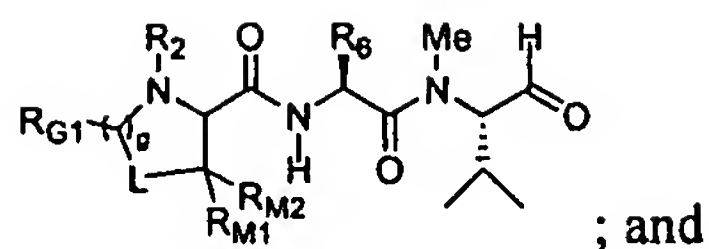
wherein any two adjacent R<sub>L1</sub>, R<sub>L2</sub>, R<sub>L3</sub>, R<sub>G1</sub>, R<sub>M1</sub> or R<sub>M2</sub> groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

79. (New) The method of claim 81 wherein the step of converting comprises steps of:

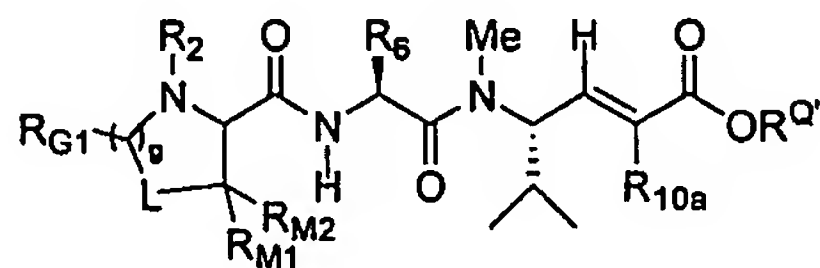
(i) subjecting the compound having the structure:



to ozonolysis conditions to form an aldehyde having the structure:



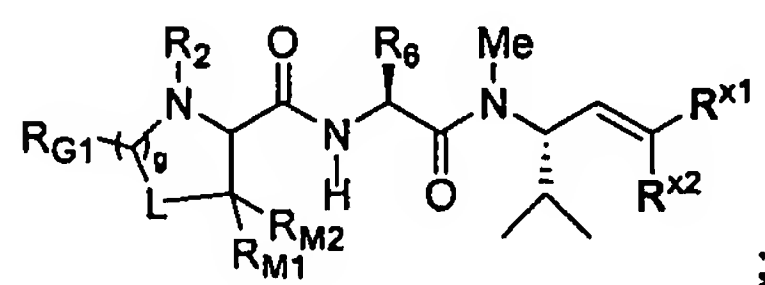
(ii) subjecting the compound formed in step (i) to suitable olefin-forming conditions to form a compound having the structure:



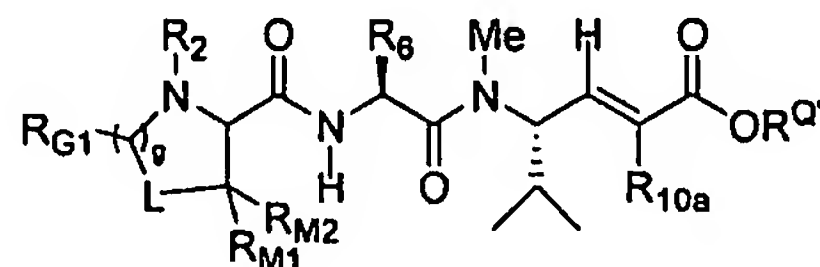
80. (New) The method of claim 81 wherein, in step (ii), the olefin-forming conditions comprise  $\text{Ph}_3\text{P}=\text{C}(\text{R}_{10a})\text{CO}_2\text{R}^{\text{Q}'}$ ; wherein  $\text{R}^{\text{Q}'}$  is hydrogen, lower alkyl or an oxygen protecting group; and  $\text{R}_{10a}$  is as defined generally above and in classes and subclasses herein.

81. (New) The method of claim 81 wherein, the step of converting comprises a step of:

subjecting the compound having the structure:



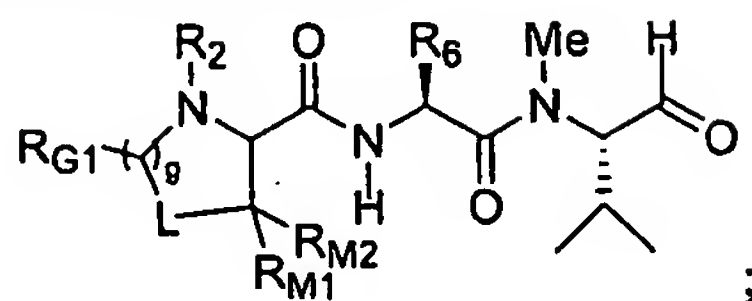
to cross-olefin-metathesis conditions in the presence of  $\text{CH}_2=\text{C}(\text{R}_{10a})\text{CO}_2\text{R}^{\text{Q}'}$  to form a compound having the structure:





**SUBSTITUTE SHEETS**

46. An intermediate having the structure:



wherein g is 1, 2, 3 or 4;

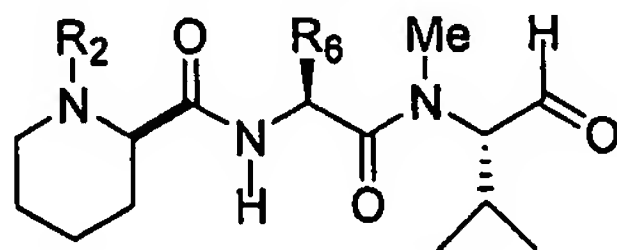
R<sub>2</sub> is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety;

R<sub>6</sub> is substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

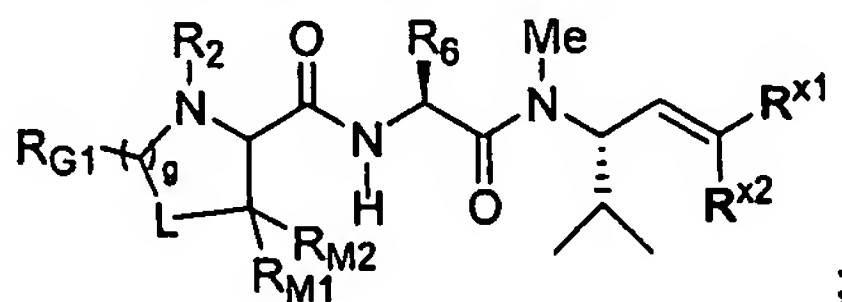
L is CR<sub>L1</sub>R<sub>L2</sub>, S, O or NR<sub>L3</sub>, wherein each occurrence of R<sub>L1</sub>, R<sub>L2</sub> and R<sub>L3</sub> is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

each occurrence of R<sub>G1</sub>, R<sub>M1</sub> and R<sub>M2</sub> is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and wherein any two adjacent R<sub>L1</sub>, R<sub>L2</sub>, R<sub>L3</sub>, R<sub>G1</sub>, R<sub>M1</sub> or R<sub>M2</sub> groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

53. The intermediate of claim 46 having the structure:



62. An intermediate having the structure:



wherein R<sup>x1</sup> and R<sup>x2</sup> are independently hydrogen, aliphatic, alicyclic or aryl;  
g is 1, 2, 3 or 4;

L is  $\text{CR}_{\text{L1}}\text{R}_{\text{L2}}$ , S, O or  $\text{NR}_{\text{L3}}$ , wherein each occurrence of  $\text{R}_{\text{L1}}$ ,  $\text{R}_{\text{L2}}$  and  $\text{R}_{\text{L3}}$  is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

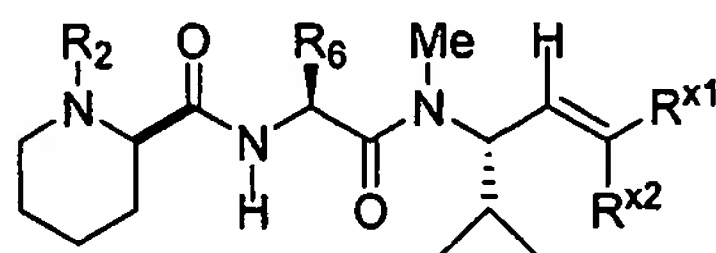
each occurrence of  $\text{R}_{\text{G1}}$ ,  $\text{R}_{\text{M1}}$  and  $\text{R}_{\text{M2}}$  is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent  $\text{R}_{\text{L1}}$ ,  $\text{R}_{\text{L2}}$ ,  $\text{R}_{\text{L3}}$ ,  $\text{R}_{\text{G1}}$ ,  $\text{R}_{\text{M1}}$  or  $\text{R}_{\text{M2}}$  groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety;

$\text{R}_2$  is hydrogen,  $-(\text{C}=\text{O})\text{R}_{\text{C}}$  or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein each occurrence of  $\text{R}_{\text{C}}$  is independently hydrogen, OH,  $\text{OR}_{\text{D}}$ , or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein  $\text{R}_{\text{D}}$  is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

$\text{R}_6$  is hydrogen,  $-(\text{C}=\text{O})\text{R}_{\text{E}}$  or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of  $\text{R}_{\text{E}}$  is independently hydrogen, OH,  $\text{OR}_{\text{F}}$ , or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; wherein  $\text{R}_{\text{F}}$  is an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety.

63. The intermediate of claim 62 having the structure:



64. The intermediate of claim 62 or 63 wherein  $\text{R}^{\text{x1}}$  and  $\text{R}^{\text{x2}}$  are independently hydrogen, alkyl or aryl.

65. The intermediate of claim 62 or 63 wherein  $\text{R}^{\text{x1}}$  and  $\text{R}^{\text{x2}}$  are each hydrogen.

66. The intermediate of any one of claims 46, 53, 62 and 63 wherein  $\text{R}_2$  is hydrogen, or a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl, heteroalkyl, -alkyl(aryl) or acyl moiety.

67. The intermediate of claim 66 wherein  $R_2$  is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl,  $-\text{CH}(\text{CH}_3)\text{Et}$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$ ,  $-\text{C}(\text{CH}_3)_2\text{Et}$ ,  $-\text{CH}(\text{CH}_3)\text{cyclobutyl}$ ,  $-\text{CH}(\text{Et})_2$ ,  $-\text{C}(\text{CH}_3)_2\text{C}\equiv\text{CH}$ , cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.
68. The intermediate of claim 66 wherein  $R_2$  is methyl, ethyl, propyl or *i*-propyl.
69. The intermediate of any one of claims 46, 53, 62 and 63 wherein  $R_6$  is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$ ,  $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ , cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl; and  $R_2$  is methyl, ethyl, propyl, butyl, pentyl, *tert*-butyl, *i*-propyl,  $-\text{CH}(\text{CH}_3)\text{Et}$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ ,  $-\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$ ,  $-\text{C}(\text{CH}_3)_2\text{Et}$ ,  $-\text{CH}(\text{CH}_3)\text{cyclobutyl}$ ,  $-\text{CH}(\text{Et})_2$ ,  $-\text{C}(\text{CH}_3)_2\text{C}\equiv\text{CH}$ , cyclohexyl, cyclopentyl, cyclobutyl or cyclopropyl.
70. The intermediate of claim 69 wherein  $R_6$  is *tert*-butyl.
71. The intermediate of any one of claims 46, 53, 62 and 63 wherein  $R_{G1}$  is hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.
72. The intermediate of claim 71 wherein  $R_{G1}$  is hydrogen, methyl or phenyl.
73. The intermediate of claim 71 wherein  $R_{G1}$  is hydrogen.
74. The intermediate of any one of claims 46, 53, 62 and 63 wherein  $R_{M1}$  and  $R_{M2}$  are each independently hydrogen, hydroxyl, a substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl moiety; a substituted or unsubstituted phenyl moiety, or  $R_{M2}$  is absent when  $R_{M1}$  and the

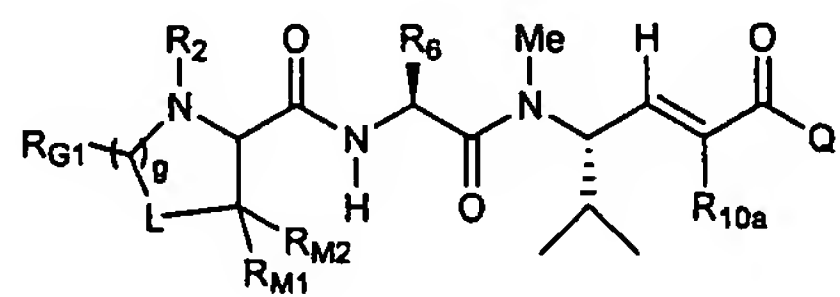
substituents on L, taken together, form a substituted or unsubstituted aryl or heteroaryl moiety.

75. The intermediate of claim 74 wherein  $R_{M1}$  and  $R_{M2}$  are each hydrogen.

76. The intermediate of any one of claims 46, 53, 62 and 63 wherein L is  $CR_{L1}R_{L2}$  wherein  $R_{L1}$  and  $R_{L2}$  are each independently hydrogen, substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl or substituted or unsubstituted phenyl.

77. The intermediate of claim 76 wherein L is  $CH_2$ .

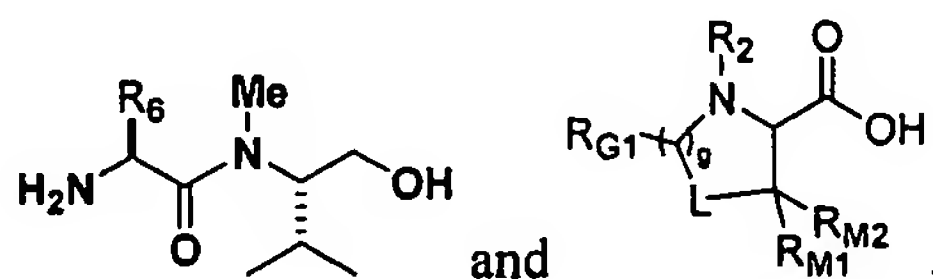
78. A method for preparing a compound of formula VI<sup>A</sup>:



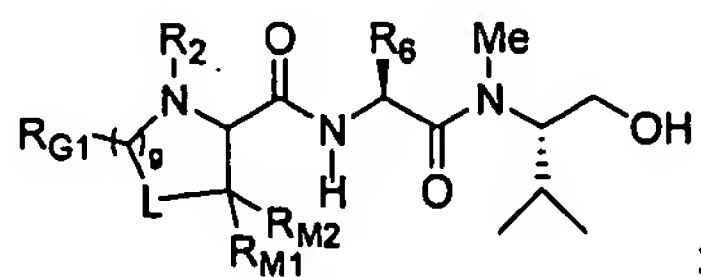
(VI<sup>A</sup>)

said method comprising steps of:

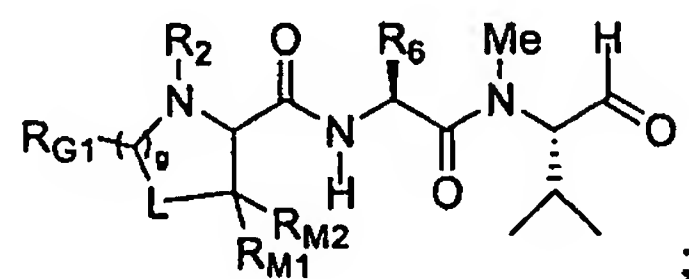
(a) reacting two compounds having the structures:



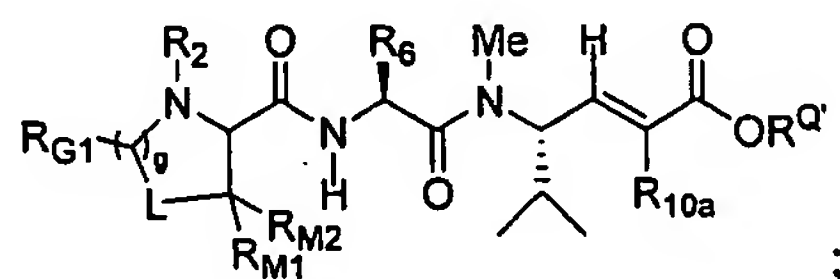
under suitable conditions to form a compound having the structure:



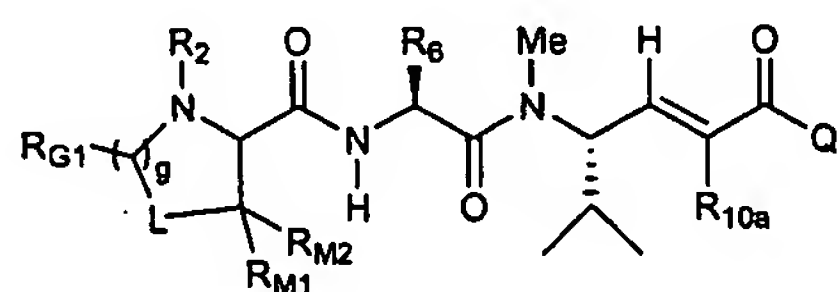
(b) oxidizing the compound formed in step (a) under suitable conditions to form a compound having the structure:



(c) subjecting the compound formed in step (b) to suitable olefin-forming conditions to form a compound having the structure:



(d) subjecting the compound formed in step (c) to suitable diversification reactions to generate the desired compound having the structure:



(VI<sup>A</sup>)

wherein g is 1 or 2;

R<sup>Q</sup> is hydrogen, lower alkyl or an oxygen protecting group;

R<sub>2</sub> and R<sub>6</sub> are independently substituted or unsubstituted linear or branched lower alkyl;

R<sub>10a</sub> is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

L is CR<sub>L1</sub>R<sub>L2</sub>, S, O or NR<sub>L3</sub>, wherein each occurrence of R<sub>L1</sub>, R<sub>L2</sub> and R<sub>L3</sub> is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

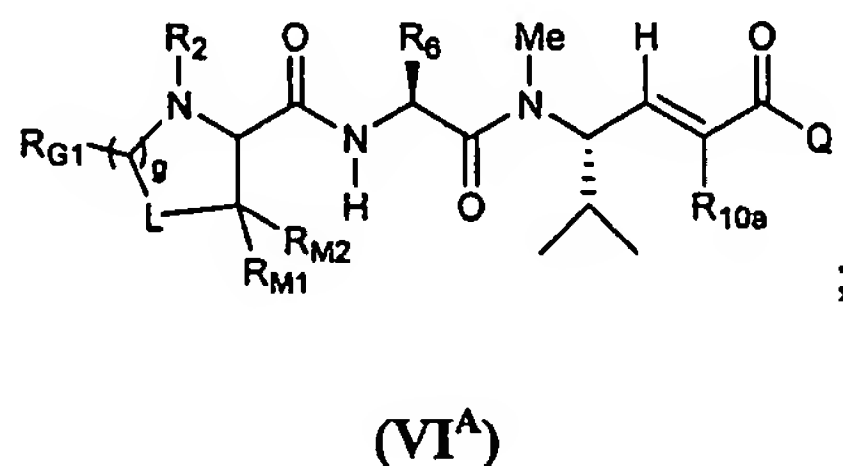
each occurrence of  $R_{G1}$ ,  $R_{M1}$  and  $R_{M2}$  is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and

wherein any two adjacent  $R_{L1}$ ,  $R_{L2}$ ,  $R_{L3}$ ,  $R_{G1}$ ,  $R_{M1}$  or  $R_{M2}$  groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

79. The method of claim 78 wherein, in the step of oxidizing, the conditions comprise Swern or Dess Martin oxidizing conditions.

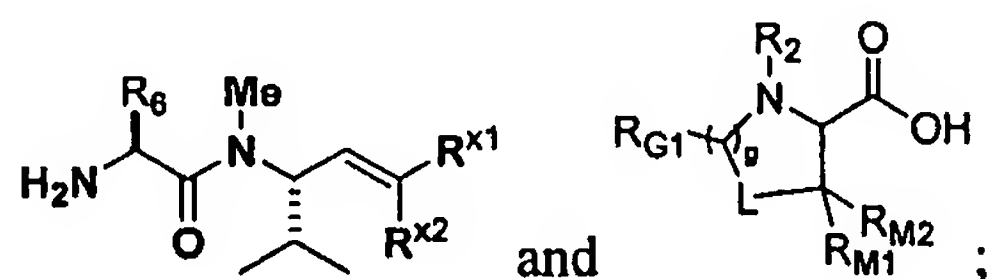
80. The method of claim 78 wherein, in step (c), the olefin-forming conditions comprise  $\text{Ph}_3\text{P}=\text{C}(\text{R}_{10a})\text{CO}_2\text{R}^{\text{Q}'}$ ; wherein  $\text{R}^{\text{Q}'}$  is hydrogen, lower alkyl or an oxygen protecting group; and  $\text{R}_{10a}$  is as defined generally above and in classes and subclasses herein.

81. A method for preparing a compound of formula  $\text{VI}^{\text{A}}$ :

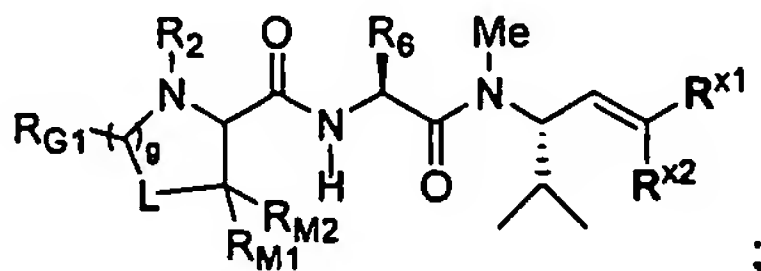


said method comprising steps of:

(a) reacting two compounds having the structures:

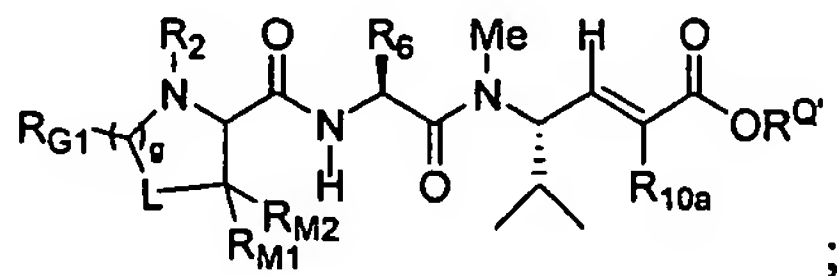


under suitable conditions to form a compound having the structure:

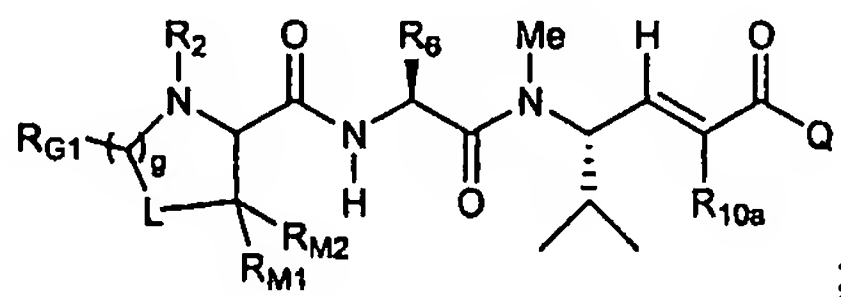


wherein  $R^{X1}$  and  $R^{X2}$  are independently hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;

(b) converting the compound formed in step (a) under suitable conditions to form a compound having the structure:



(c) subjecting the compound formed in step (b) to suitable diversification reactions to generate the desired compound having the structure:



(VI<sup>A</sup>)

wherein  $g$  is 1 or 2;

$R^Q$  is hydrogen, lower alkyl or an oxygen protecting group;

$R_2$  and  $R_6$  are independently substituted or unsubstituted linear or branched lower alkyl;

$R_{10a}$  is hydrogen or substituted or unsubstituted, linear or branched, cyclic or acyclic, or saturated or unsaturated lower alkyl;

$L$  is  $CR_{L1}R_{L2}$ ,  $S$ ,  $O$  or  $NR_{L3}$ , wherein each occurrence of  $R_{L1}$ ,  $R_{L2}$  and  $R_{L3}$  is independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

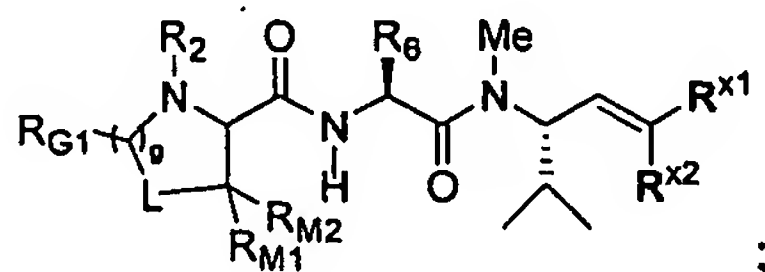
each occurrence of  $R_{G1}$ ,  $R_{M1}$  and  $R_{M2}$  is each independently hydrogen or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and



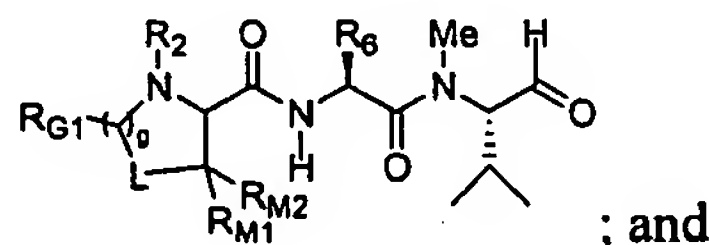
wherein any two adjacent  $R_{L1}$ ,  $R_{L2}$ ,  $R_{L3}$ ,  $R_{G1}$ ,  $R_{M1}$  or  $R_{M2}$  groups, taken together, form a substituted or unsubstituted alicyclic or heteroalicyclic moiety containing 3-6 atoms or an aryl or heteroaryl moiety.

79. The method of claim 81 wherein the step of converting comprises steps of:

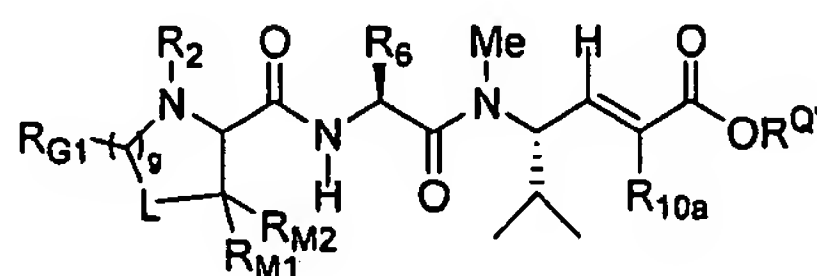
(i) subjecting the compound having the structure:



to ozonolysis conditions to form an aldehyde having the structure:



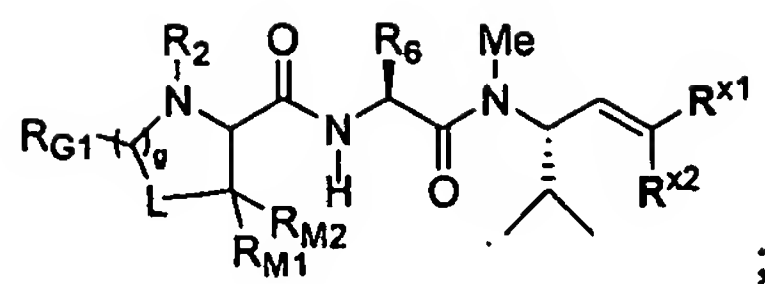
(ii) subjecting the compound formed in step (i) to suitable olefin-forming conditions to form a compound having the structure:



80. The method of claim 81 wherein, in step (ii), the olefin-forming conditions comprise  $Ph_3P=C(R_{10a})CO_2R^{Q'}$ ; wherein  $R^{Q'}$  is hydrogen, lower alkyl or an oxygen protecting group; and  $R_{10a}$  is as defined generally above and in classes and subclasses herein.

81. The method of claim 81 wherein, the step of converting comprises a step of:

subjecting the compound having the structure:



to cross-olefin-metathesis conditions in the presence of  $\text{CH}_2=\text{C}(\text{R}_{10a})\text{CO}_2\text{R}^Q$  to form a compound having the structure:

